An official website of the United States government
Here's how you know

FEBRUARY 28, 2023

Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with SARS-CoV-2 Infection 2023 Case Definition

NOTE: A surveillance case definition is a set of uniform criteria used to define a disease for public health surveillance. Surveillance case definitions enable public health officials to classify and count cases consistently across reporting jurisdictions. Surveillance case definitions are not intended to be used by healthcare providers for making a clinical diagnosis or determining how to meet an individual patient's health needs.

CSTE Position Statement(s)

22-ID-02

Multisystem inflammatory syndrome in children (MIS-C) associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is a severe delayed hyperinflammatory condition in children and adolescents occurring 2–6 weeks after antecedent SARS-CoV-2 infection.[1,2] First described in the United Kingdom in April 2020, MIS-C was soon identified in the United States.[3,4] Although acute SARS-CoV-2 infection in children is generally mild or asymptomatic,[5] associated MIS-C is characterized by fever, elevated laboratory markers of systemic inflammation, and multiple organ system dysfunction including cardiovascular, mucocutaneous, gastrointestinal, hematologic, neurologic, and renal involvement.[2,6] Some patients with MIS-C may also present with respiratory failure or radiographic pulmonary abnormalities indicative of pulmonary inflammation, a phenotypic overlap with Coronavirus Disease 2019 (COVID-19) viral pneumonia, or cardiogenic pulmonary edema.[6,7,8] Patients with MIS-C are often critically ill, with the majority requiring admission to an intensive care unit (ICU) and 1–3% requiring extracorporeal membrane oxygenation (ECMO).[2,6,9] Mortality among MIS-C patients has been estimated to be 1–2%.[6,9,10]

Using the case definition released by the Centers for Disease Control and Prevention (CDC) in May 2020, incidence of MIS-C in seven U.S. jurisdictions during April–June 2020 was estimated to be 5.1 cases per million person-months or 316 cases per million SARS-CoV-2 infections among persons aged <21 years.[11] Both measures of MIS-C incidence decreased with age and were higher among non-Hispanic Black, Hispanic, and non-Hispanic Asian or Pacific Islander persons, compared with non-Hispanic White persons.[11]These results corroborate other results demonstrating disproportionate MIS-C burden among Black and Hispanic persons early in the pandemic.[12,13] However, children and adolescents diagnosed with MIS-C appear less likely to have underlying medical conditions than those diagnosed with COVID-19.[6]

Comparative cohort studies of MIS-C and acute pediatric COVID-19 have suggested that mucocutaneous, cardiovascular, and hematologic organ system involvement, as well as the presence of abdominal pain, vomiting, or diarrhea are features that raise the likelihood of a diagnosis of MIS-C.[6,8,14] However, the prevalence of renal and neurologic involvement appears to be similar in MIS-C and COVID-19.[6,15] Further, respiratory organ system involvement is more common in COVID-19 than in MIS-C and its inclusion in the MIS-C case definition may contribute to misclassification.[8,14]

Position statement 22-ID-02 establishes a standardized case definition for MIS-C associated

through consultation with clinical experts, review of the published literature, and interrogation of the national MIS-C surveillance data collected using the 2020 CDC MIS-C case definition, and data collected through the Overcoming COVID-19 network MIS-C registry. [1,6,9]

Clinical Criteria

An illness in a person aged <21 characterized by all of the following, in the absence of a more likely alternative diagnosis*:

- Subjective or documented fever (temperature ≥38.0º C)

  AND

- Clinical severity requiring hospitalization or resulting in death

  AND

- Evidence of systemic inflammation indicated by C-reactive protein ≥3.0 mg/dL (30 mg/L)

  AND

- New onset manifestations in at least two of the following categories:

  1. Cardiac involvement indicated by:
     - Left ventricular ejection fraction <55%, **OR**
     - Coronary artery dilatation, aneurysm, or ectasia, **OR**
     - Troponin elevated above laboratory normal range, or indicated as elevated in a clinical note
  2. Mucocutaneous involvement indicated by:
     - Rash, **OR**
     - Inflammation of the oral mucosa (e.g., mucosal erythema or swelling, drying or fissuring of the lips, strawberry tongue), **OR**

- Extremity findings (e.g., erythema [redness] or edema [swelling] of the hands or feet)

3. Shock**

4. Gastrointestinal involvement indicated by:

   - Abdominal pain, **OR**
   - Vomiting, **OR**
   - Diarrhea

5. Hematologic involvement indicated by:

   - Platelet count <150,000 cells/μL **OR**
   - Absolute lymphocyte count (ALC) <1,000 cells/μL

*If documented by the clinical treatment team, a final diagnosis of Kawasaki Disease should be considered an alternative diagnosis. These cases should not be reported to national MIS-C surveillance.

** Clinician documentation of shock meets this criterion.

Laboratory Criteria

Confirmatory laboratory evidence:

- Detection of SARS-CoV-2 ribonucleic acid (RNA) in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen using a diagnostic molecular amplification test (e.g., polymerase chain reaction [PCR]), **OR**
- Detection of SARS-CoV-2 specific antigen in a clinical specimen*** up to 60 days prior to or during hospitalization, or in a post-mortem specimen, **OR**
- Detection of SARS-CoV-2 specific antibodies^ in serum, plasma, or whole blood associated with current illness resulting in or during hospitalization

****Positive molecular or antigen results from self-administered testing using over-the-*

^Includes a positive serology test regardless of COVID-19 vaccination status. Detection of anti-nucleocapsid antibody is indicative of SARS-CoV-2 infection, while anti-spike protein antibody may be induced either by COVID-19 vaccination or by SARS-CoV-2 infection.

Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.

Epidemiologic Linkage

Close contact‡ with a confirmed or probable case of COVID-19 disease in the 60 days prior to hospitalization.

‡Close contact is generally defined as being within 6 feet for at least 15 minutes (cumulative over a 24-hour period). However, it depends on the exposure level and setting; for example, in the setting of an aerosol-generating procedure in healthcare settings without proper personal protective equipment (PPE), this may be defined as any duration.

Criteria to Distinguish a New Case from an Existing Case

A case should be enumerated as a new case if the person had never previously been enumerated as a case **OR** if the person was most recently enumerated as a case with illness onset date (if available) or hospital admission date >90 days prior.

Case Classification

Suspect

- Meets the vital records criteria.

Probable

- Meets the clinical criteria **AND** the epidemiologic linkage criteria.

Confirmed

National Notifiable Diseases Surveillance System (NNDSS) MENU

Other Criteria

Vital Records Criteria

A person aged <21 years whose death certificate lists MIS-C or multisystem inflammatory syndrome as an underlying cause of death or a significant condition contributing to death.

Case Classification Comments

Note: For cases initially identified as suspect, jurisdictions may conduct investigation of clinical and laboratory records to determine if confirmed or probable case criteria are met.

Comment: To provide consistency in case classification, review of case information and assignment of final case classification for all suspected MIS-C cases will be done by experts in national MIS-C surveillance.

Related Materials

Council of State and Territorial Epidemiologists/CDC Surveillance Case Definition for Multisystem Inflammatory Syndrome in Children Associated with SARS-CoV-2 Infection — United States

References

1. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. *N Engl J Med* 2020; 383(4): 334-46.

2. Belay ED, Abrams J, Oster ME, et al. Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic. *JAMA Pediatr* 2021.

3. Dufort EM, Koumans EH, Chow EJ, et al. Multisystem Inflammatory Syndrome in Children in New York State. *N Engl J Med* 2020; 383(4): 347-58.

4. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 2020; 395(10237): 1607-8.

5. Castagnoli R, Votto M, Licari A, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review. *JAMA Pediatr* 2020; 174(9): 882-9.

6. Feldstein LR, Tenforde MW, Friedman KG, et al. Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19. *JAMA* 2021; 325(11): 1074-87.

7. Gotzinger F, Santiago-Garcia B, Noguera-Julian A, et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. *Lancet Child Adolesc Health* 2020; 4(9): 653-61.

8. Godfred-Cato S, Abrams JY, Balachandran N, et al. Distinguishing Multisystem Inflammatory Syndrome in Children From COVID-19, Kawasaki Disease and Toxic Shock Syndrome. *Pediatr Infect Dis J* 2022; 41(4): 315-23.

9. Miller AD, Zambrano LD, Yousaf AR, et al. Multisystem Inflammatory Syndrome in Children-United States, February 2020-July 2021. *Clin Infect Dis* 2021.

10. Bowen A, Miller AD, Zambrano LD, et al. Demographic and Clinical Factors Associated With Death Among Persons <21 Years Old With Multisystem Inflammatory Syndrome in Children-United States, February 2020-March 2021. *Open Forum Infect Dis* 2021; 8(8): ofab388.

11. Payne AB, Gilani Z, Godfred-Cato S, et al. Incidence of Multisystem Inflammatory Syndrome in Children Among US Persons Infected With SARS-CoV-2. *JAMA Network Open* 2021; 4(6): e2116420-e.

12. Lee EH, Kepler KL, Geevarughese A, et al. Race/Ethnicity Among Children With COVID-19-Associated Multisystem Inflammatory Syndrome. *JAMA Netw Open* 2020; 3(11):e2030280.

13. Javalkar K, Robson VK, Gaffney L, et al. Socioeconomic and Racial and/or Ethnic Disparities in Multisystem Inflammatory Syndrome. *Pediatrics* 2021; 147(5).

14. Geva A, Patel MM, Newhams MM, et al. Data-driven clustering identifies features distinguishing multisystem inflammatory syndrome from acute COVID-19 in children and adolescents. *EClinicalMedicine* 2021; 40: 101112.

15. [illegible]

Syndrome. *JAMA Neurol* 2021; 78(5): 536-47.

SOURCES SHARE

CONTENT SOURCE:

National Notifiable Diseases Surveillance System (NNDSS) >

NNDSS receives and shares case data from state, local, and territorial health departments to help public health monitor, control, and prevent serious diseases.

View All >

About About National Notifiable Diseases Surveillance System

What is Case Surveillance?

Case Surveillance Modernization

Infectious Disease Tables
Non-Infectious Disease Data

Technical Resource Center

Case Surveillance in Action

Contact Us

VIEW ALL >

Sign up for Email Updates >